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Case Report: Leptospirosis by Wild Rat Bite in Winter in Tokyo Metropolitan Area, Japan

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Abstract. We report a case of leptospirosis in Tokyo in winter due to a rat bite, an uncommon cause of *Leptospira* infection. In Japan, many cases due to exposure to fresh water have been reported from domestic southwest islands in summer. However, a previous report on leptospirosis in Tokyo documented several cases occurring in winter. The main route of infection in the Tokyo metropolitan area during winter was attributed to the increased chance of direct rat exposure. Rapid and feasible diagnostic methods are needed to elucidate its epidemiology and provide prompt treatment.

INTRODUCTION

Leptospirosis is a zoonosis caused by *Leptospira* spp. *Leptospira* spp. settle in the rodents' kidney tubules and are discharged in urine.[1] Thus, leptospirosis is typically caused by percutaneous contact with the sewage and soil, contaminated with rodent urine. However, *Leptospira* spp. are rarely detected in rodent saliva.[2] There have been limited reports of leptospirosis from rat bites.[3,4] We report a case of severe leptospirosis, caused by a wild rat bite.

Leptospirosis is prevalent in developing countries in tropical and subtropical regions.[5] In Japan, many cases have been reported from Okinawa Prefecture, which is located southwest. Since nature tourism is a significant industry in the area, the leptospirosis cases were typically caused by leisure or work activities, involving exposure to fresh water during the summer.[6] We encountered an interesting case occurring in the Tokyo metropolitan area during the winter.

CASE

A 60-year-old previously healthy man came to the clinic with general malaise, abdominal pain, and jaundice. Three weeks prior to his admission, his fingers were bitten by a wild rat, which he caught in the dishwashing area. Two weeks before admission, he experienced bilateral lower leg pain and gradually worsening malaise. Four days before admission, he sought medical care in a nearby clinic, and he started oral amoxicillin 250 mg three times a day. At that time, his platelet level was 45,000/μL, and C-reactive protein (CRP) was 29.0 mg/dL. He was referred to our hospital for further management and treatment. He had no history of traveling abroad, or wading in flood water, rice paddies, or swamps within the past month. He also wore rubber boots while working, and had no direct contact with drainage or other bodies of water in his workplace.

On admission, the patient appeared generally well. He required 1 L of nasal oxygen, but his other vital signs were stable. Physical examination revealed jaundice and bite marks on his fingers. Blood tests showed acute liver injury (total bilirubin 22.5 mg/dL, direct bilirubin 17.4 mg/dL, aspartate aminotransferase 81 U/L, alanine transaminase 139 U/L, lactate dehydrogenase 576 U/L), acute kidney injury (blood urea nitrogen of 119.3 mg/dL and creatinine of 3.26 mg/dL), elevated inflammation (CRP of 6.78 mg/dL), and thrombocytopenia (platelet 56,000/μL). Computed tomography showed ground-glass appearance in both the lung fields, which was consistent with alveolar hemorrhage. Leptospirosis was strongly suspected, and the patient was treated with ceftriaxone (2 g) every 24 hours. Systemic corticosteroid therapy was not administered because of the rapid improvement of the patient's symptoms, general condition, and laboratory findings compared with when he appeared in the nearby clinic. After admission, his acute kidney injury and thrombocytopenia improved, and he no longer required oxygen supplementation.

The *Leptospira* flagellar gene *flaB* was amplified in the urine, collected the day after admission. By determining the sequence of the *flaB* amplicon, *L. interrogans* was identified (DDBJ accession number LC671662). The results of the microscopic agglutination test showed a significant increase in antibody titers against *L. interrogans* serovar Copenhageni in paired sera on admission and 20 days later. This confirmed an infection, caused by *L. interrogans* serogroup Icterohaemorrhagiae. The antimicrobial agents were discontinued on the sixth day due to drug eruptions. The patient had a favorable clinical course, and he was discharged from hospital on day 10.

DISCUSSION

We report a case of severe leptospirosis caused by a wild rat bite in the Tokyo metropolitan area. In a previous study, *Leptospira* spp. were detected in 17% of rats in Tokyo.[7] This included the serogroup Icterohaemorrhagiae, which was confirmed in this case. Theoretically, it may be possible that disruption of skin barrier due to rat bite was exposed to the *Leptospira*-contaminated water. However, the patient was aware of the rat bite, and therefore it would be unexpected to expose the bitten finger into the wastewater. Also, exposure to wastewater contaminated with rat urine was unlikely, because he wore rubber boots. Thus, the rat bite in his workplace was the most likely cause of *Leptospira* infection.

Leptospira spp. settle in the host animals' kidney tubules and are excreted through the urine.[1] However, they are rarely excreted in the saliva.[2] According to previous reports, rats, temporarily harboring leptospires in the oral cavity due to pubic grooming, can transmit *Leptospira* spp. to humans

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through a bite wound.[3,4] The *L. interrogans* infection in this case likely occurred via a similar mechanism.

In Japan, leptospirosis typically occurs from July to October.[6] This reflects the possible opportunities for exposure, such as leisure activities by the rivers and flooding caused by typhoons. However, a previous report on leptospirosis in Tokyo documented several cases occurring in winter.[8] Direct exposure to rats was reportedly a risk factor for leptospirosis in urban areas, and the disease can occur during any season. These findings were consistent with the present case, wherein the patient was bitten by a rat in January. Direct rat exposure in the Tokyo metropolitan area increases during the winter. Further case reports are needed to prove this hypothesis.

We reported a case of leptospirosis caused by a wild rat bite in the Tokyo metropolitan area. Since rat bites induce nonspecific constitutional symptoms, rat-bite fever should be considered the leading differential diagnosis. Leptospirosis can also occur due to rat bites, even in areas where leptospirosis is not prevalent. Thus, clinicians should consider leptospirosis in all patients who were bitten by rats. During winter, rat bites were the main cause of *Leptospira* infection. Antibiotics prevent severe leptospirosis progression.[9] A diagnostic method should be established to facilitate early diagnosis and therapeutic intervention. It is also necessary to clarify the epidemiology and characteristics of leptospirosis.

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